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10/579,225	03/24/2008	Risto Kostiainen	Q94898	6385

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EXAMINER	
IPPOLITO RAUSCH, NICOLE	
ART UNIT	PAPER NUMBER
2881	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/579,225	KOSTIAINEN ET AL.	
	Examiner	Art Unit	
	NICOLE IPPOLITO RAUSCH	2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29 and 33-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed 4/29/2010 have been fully considered but they are not persuasive. Specifically, in respect to claim 1, the applicant argues that Miller fails to teach APCI. In one sense, that is somewhat irrelevant as applies to claim 1, as claim 1 does not disclose APCI. But furthermore, Miller does teach APCI as an alternative embodiment, which the applicant does in fact acknowledge on page 12 of their "Remarks". Thus Miller does teach APCI, and as the invention of Miller teaches a micromechanical structure, Miller covers the limitation of APCI. Similarly, Syms teaches a monolithic miniaturized device, which specifically teaches a corona discharge. The Applicant acknowledges as much at the bottom of page 12 of their "Remarks", and as such, the examiner cannot understand how the Applicant holds that Syms does not teach corona discharge, merely because (on page 13 of the "Remarks" section) "..nowhere else in the reference does Syms refer to either a glow or corona.". It is not, required that Syms discuss this further, or in great detail, later in the reference. The Applicant agrees that Syms does teach it, and as such, this is sufficient. Further, in regards to claim 4, again, Syms teaches a single monolithic structure including corona discharge, as acknowledged by the Applicant. Thus again, the examiner fails to understand how Miller and Syms, alone or in combination, fails to teach the APCI and corona discharge of the independent and discussed dependent claims.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 2, 3, 4, 5, 6, 7, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 27, 28 and 29 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (U.S. Patent Application Publication Number 20030146377, from hereinafter “Miller”) in view of Syms (U.S. Patent Number 7208729, from hereinafter “Syms”).

5. In regards to claim 1, Miller teaches that a solution to be examined is vaporized in a vaporizer (paragraphs 0126, 0128, FIG. 3A paragraphs 0124-0125 discloses heating the flow path, that will lead to vaporization from the heat, furthermore it is an electrospray tip and hence nebulizing takes place), the vaporized sample solution is sprayed using a gas flow (FIG. 13B, tip 20, gas flow 90, paragraph 0154), the ions are

separated and directed to a detector (see, i.e., paragraph 0002), and that the vaporizer is fabricated as a micromechanical structure (see, i.e., paragraph 0134).

In regards to claim 1, Miller fails to explicitly teach that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. However, Miller does teach electrodes immediately outside of the spray region, which could serve to cause corona discharge-assisted ionization (FIG. 13, electrodes 104, paragraph 0154).

Syms teaches that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions (column 4 lines 50-55).

In view of the teaching of Syms it would have been obvious to one of ordinary skill in the art at the time the invention was made that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. Corona discharge may serve to heighten the ionization effect, allowing for a better sample that should, in turn, allow for a clearer, more defined mass peak in the final mass analysis.

6. In regards to claim 2, Miller teaches that a vaporizer is used which comprises flow channel networks for the solution and the carrier gas possibly used for feeding the solution (paragraphs 0051, 0061, etc., FIGS. 13, 16, paragraph 0154, etc.), as well as a heater of the vaporizer, which are all included in the monolithic structure (Miller states that this is a MEMS device in, i.e., paragraph 0134, which means that all of the components are integrated on the monolithic structure).

7. In regards to claim 4, though Miller as modified by Syms fails to explicitly teach that the vaporizer and corona discharge zone are integrated into a single micromechanical structure, it would have been obvious. Both Miller and Syms disclose monolithic micromechanical structures that work in mass spectrometry application. Hence, any variation of either Miller or Syms would be modified in such a way that the device continues to be a monolithic micromechanical structure that allows for portability of the device if desired/required.

8. In regards to claim 5, Miller teaches that the micromechanical structure used comprises flow channel networks designed for one or more wafers, and a heater (FIGS. 4A-C, 11, etc. illustrate that it is a wafer structure-that is what a MEMS device is-paragraph 0137, for example, discusses flow channels, paragraph 0125 discusses the onboard heaters that assist in desolvation of the sample).

9. In regards to claim 6, Miller teaches a substrate wafer in which flow channel networks for liquid and gases are formed (see, i.e. FIGS. 4A-D, FIG. 11A, 13-13, etc.) and a cover wafer, attached to the substrate in which a heater for vaporizing the sample solution is patterned (heaters are discussed in paragraph 0153-0156, for instance, while FIG. 4B illustrates the wafer 'sectioning').

10. In regards to claim 7, Miller teaches that the vaporized sample is ionized in the presence of air, at normal atmospheric pressure (see, i.e., paragraph 0059).

In regards to claim 7, Miller fails to explicitly teach that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. However, Miller does teach electrodes

immediately outside of the spray region, which could serve to cause corona discharge-assisted ionization (FIG. 13, electrodes 104, paragraph 0154).

Syms teaches that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions (column 4 lines 50-55).

In view of the teaching of Syms it would have been obvious to one of ordinary skill in the art at the time the invention was made that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. Corona discharge may serve to heighten the ionization effect, allowing for a better sample that should, in turn, allow for a clearer, more defined mass peak in the final mass analysis.

11. In regards to claim 10, Miller teaches that polar compounds, non-polar compounds, neutral compounds or ionic compounds are examined, and the sample to be examined is dissolved in a polar or non-polar solvent, used as an eluent, to generate the sample solution (paragraph 0177).

12. In regards to claim 11, Miller as modified by Syms fails to explicitly teach that the molar masses are at most 2000 Da. However it would have been obvious to one of ordinary skill in the art at the time the invention was made that the molar masses are at most 2000 Da, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. See in re Aller, 105 USPQ 233.

13. In regards to claim 13, Miller teaches that the sample is ionized using the APCI method (see, i.e., paragraph 0059).

14. In regards to claim 14, Miller teaches that the gas flow used for the injection is brought in essentially perpendicular to the flow direction of the sample (see, i.e., FIG. 13A, paragraph 0154).

15. In regards to claim 15, Miller teaches that the gas flow is fed into the device in the flow direction of the liquid and before the feed opening of the liquid (see, i.e., FIG. 13A, paragraph 0154).

16. In regards to claim 16, Miller teaches that the gas flow is fed through one feed opening, in order to distribute the gas flow around the liquid flow comprising sample, and, as a result, a homogenous mixture is achieved (see FIG. 13a, for example).

17. In regards to claim 17, Miller teaches that a solution to be examined is vaporized in a vaporizer (paragraphs 0126, 0128, FIG. 3A paragraphs 0124-0125 discloses heating the flow path, that will lead to vaporization from the heat, furthermore it is an electrospray tip and hence nebulizing takes place), that the sample is ionized using APCI (see, i.e., paragraph 0059) a detector to detect the ions (see, i.e., paragraph 0002) a means for directing the charged particles into the detector (FIG. 13A, attractor electrodes 104, paragraph 0154), and that the vaporizer is fabricated as a micromechanical structure (see, i.e., paragraph 0134).

In regards to claim 17, Miller fails to explicitly teach that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. However, Miller does teach electrodes

immediately outside of the spray region, which could serve to cause corona discharge-assisted ionization (FIG. 13, electrodes 104, paragraph 0154).

Syms teaches that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions (column 4 lines 50-55).

In view of the teaching of Syms it would have been obvious to one of ordinary skill in the art at the time the invention was made that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. Corona discharge may serve to heighten the ionization effect, allowing for a better sample that should, in turn, allow for a clearer, more defined mass peak in the final mass analysis.

18. In regards to claim 18, Miller teaches that a vaporizer is used which comprises flow channel networks for the solution and the carrier gas possibly used for feeding the solution (paragraphs 0051, 0061, etc., FIGS. 13, 16, paragraph 0154, etc.), as well as a heater of the vaporizer, which are all included in the monolithic structure (Miller states that this is a MEMS device in, i.e., paragraph 0134, which means that all of the components are integrated on the monolithic structure).

19. In regards to claim 20, though Miller as modified by Syms fails to explicitly teach that the vaporizer and corona discharge zone are integrated into a single micromechanical structure, it would have been obvious. Both Miller and Syms disclose monolithic micromechanical structures that work in mass spectrometry application. Hence, any variation of either Miller or Syms would be modified in such a way that the

device continues to be a monolithic micromechanical structure that allows for portability of the device if desired/required.

20. In regards to claim 21, Miller teaches that there is a monolithic block which is formed in two or more parts which are connected to each other (see, i.e., FIG. 4B).

21. In regards to claim 27, Miller teaches that the flow channel system of the carrier gas used for feeding the solution is connected to a feed nozzle gas, which nozzle is located upstream in the flow direction of the solution and through which gas can be fed essentially perpendicular to the flow direction of the solution (see, i.e., FIG. 13A).

22. In regards to claim 28, Miller teaches that the gas flow is fed through one feed opening, in order to distribute the gas flow around the liquid flow comprising sample, and, as a result, a homogenous mixture is achieved (see FIG. 13a, for example).

23. In regards to claim 29, Miller teaches that the heater comprises heating resistors, the foreparts of which are made wide in order to decrease the flow resistance (FIG. 4A, heating resistors 53r, 55r, paragraph 0124). Though Miller as modified by Syms fails to teach that the resistors are made narrow near the mixing zone of the gas and liquid, it would have been an obvious variant. Doing so would generate a more intense localized heating, if so desired, and perhaps create a more perfect ionization of the sample, thus improving the sample overall and theoretically improving the final mass determination of the sample.

24. In regards to claims 3, 12 and 19, Miller as modified by Syms teaches the invention except for the flow rate ranges of the liquids and gases in the system. It would have been obvious to one of ordinary skill in the art at the time the invention was made

to use the disclosed ranges in the instant application, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. See in re Aller, 105 USPQ 233. In this instance, the ranges would have to be optimized such that the desired flow of ions are achieved, however, somewhat limited as well. Too high a flow rate could well cause too much pressure inside of the micromechanical device, which could in principle blow it to pieces. Thus, maximizing the flows for the correct ion rate while keeping the rates low enough to avoid damaging the device would have been obvious.

25. In regards to claim 34, Miller teaches that a solution to be examined is vaporized in a vaporizer (paragraphs 0126, 0128, FIG. 3A paragraphs 0124-0125 discloses heating the flow path, that will lead to vaporization from the heat, furthermore it is an electrospray tip and hence nebulizing takes place), that the sample is ionized using APCI (see, i.e., paragraph 0059) a detector to detect the ions (see, i.e., paragraph 0002) a means for directing the charged particles into the detector (FIG. 13A, attractor electrodes 104, paragraph 0154), and that the vaporizer is fabricated as a micromechanical structure (see, i.e., paragraph 0134).

In regards to claim 34, Miller fails to explicitly teach that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. However, Miller does teach electrodes immediately outside of the spray region, which could serve to cause corona discharge-assisted ionization (FIG. 13, electrodes 104, paragraph 0154).

Syms teaches that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions (column 4 lines 50-55).

In view of the teaching of Syms it would have been obvious to one of ordinary skill in the art at the time the invention was made that the sample is placed into a corona discharge zone, where the sample to be ionized is ionized using a corona discharge to generate gas phase ions. Corona discharge may serve to heighten the ionization effect, allowing for a better sample that should, in turn, allow for a clearer, more defined mass peak in the final mass analysis.

26. In regards to claims 33 and 36-37, Miller as modified by Syms fails to explicitly teach that the molar masses of the examined compounds are at most 1000 Daltons, or that the flow channels are dimensioned so that the volume of the liquid flow passing through them is less than 10 uL/min. However, this would have been obvious to one of ordinary skill in the art at the time the invention was made. Such a small, micromechanical structure is unlikely to be able to support large sample masses, or high flow rates without destroying the structure from the pressure. In the interest of minimizing these values to protect the device, it would have been obvious.

27. In regards to claim 35, Miller as modified by Syms fails to explicitly teach that However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the flow channel system includes a wedge-shaped guide which form a tapering hole at the discharge end. So doing creates a finer spray which allows

for the corona discharge to act more effectively, thus allowing for a more complete ionization of the sample and a more thorough mass determination to be made.

28. Claims 8-9 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller as modified by Syms as applied to claims 1 and 17 above, and further in view of Guevremont et al. (U.S. Patent Application Publication Number 20060151694, from hereinafter "Guevremont"). The teachings of Miller and Syms have been discussed above.

29. In regards to claims 8 and 24, Miller as modified by Syms does teach that the corona discharge zone comprises a needle-shaped electrode (see, i.e., FIG. 13a). However, it is not explicitly taught that the needle is connected to a voltage which is so high in relation to the curtain plate of the mass spectrometer that the electric field strength, at least in the immediate vicinity of the tip, exceeds the corona discharge threshold of air.

Guevremont teaches that the needle is connected to a voltage which is so high in relation to the curtain plate of the mass spectrometer that the electric field strength, at least in the immediate vicinity of the tip, exceeds the corona discharge threshold of air (paragraph 0142).

In view of the teaching of Guevremont it would have been obvious to one of ordinary skill in the art at the time the invention was made that the needle is connected to a voltage which is so high in relation to the curtain plate of the mass spectrometer that the electric field strength, at least in the immediate vicinity of the tip, exceeds the corona discharge threshold of air. If this were not the case, ions would not be formed in

the corona discharge region. Furthermore, the curtain plate would, if set to high, act to further ionize the ions (i.e. create fragments) which may not be desirable, if the voltage were set at too high of a value.

30. In regards to claims 9 and 25, Miller as modified by Syms and Guevremont as discussed above fails to teach that the curtain plate is set to at least 1 kV, while the field strength near the tip of the electrode is set to 50 kV/mm.

However, Guevremont does teach that the curtain plate is set to at least 1 kV, while the field strength near the tip of the electrode is set to 50 kV/mm (paragraph 0142, the entire needle is set at 3 kV, but it is likely to be several millimeters to even inches in length, and hence at the tip, a concentration of 50 kV/mm is possible).

In view of this further teaching of Guevremont it would have been obvious to one of ordinary skill in the art at the time the invention was made that the curtain plate is set to at least 1 kV, while the field strength near the tip of the electrode is set to 50 kV/mm. If this were not the case, ions would not be formed in the corona discharge region. Furthermore, the curtain plate would, if set to high, act to further ionize the ions (i.e. create fragments) which may not be desirable, if the voltage were set at too high of a value.

31. Claims 22-23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller as modified Syms as applied to claim 21 above, and further in view of Apffel et al. (U.S. Patent Number 6649908, from hereinafter “Apffel”). The teachings of Miller and Syms have been discussed above.

32. In regards to claim 22, Miller does teach that the gas and liquid flows channels are formed in a silicon wafer (paragraph 0121). However, Miller as modified by Syms fails to teach that the heater is formed in glass.

Apffel teaches that the device may be formed in glass (columns 6-7).

In view of the teaching of Apffel it would have been obvious to one of ordinary skill in the art at the time the invention was made that the heater is formed in glass. Glass is less likely to be damaged from the heat exposure than silicon, as it is a more effective insulator, and so to prevent possible damage to the device, this would have been obvious.

33. In regards to claim 23, Miller teaches that the heater for vaporization is formed in silicon (see, i.e., paragraph 0121. Realistically, wafers usually are made from silicon).

In regards to claim 23, Miller as modified by Syms fails to teach that the gas and liquid flows channels are formed from glass.

Apffel teaches that the gas and liquid flows channels are formed from glass (columns 6-7).

In view of the teaching of Apffel it would have been obvious to one of ordinary skill in the art at the time the invention was made that the gas and liquid flows channels are formed from glass. Glass has a lower coefficient of friction then silicon, and so, the materials will be able to flow more smoothly as a result.

34. In regards to claim 26, Miller as modified by Syms and Apffel fails to explicitly teach that the entire device is fabricated from glass. However, in view of the teaching of Apffel (columns 6-7) it would have been obvious. Glass allows for easier flow of the

sample materials, while the higher melting point should act to ensure that no damage due to heating the device occurs. In the interest of creating longevity of the device, this would have been obvious.

Conclusion

35. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE IPPOLITO RAUSCH whose telephone number is (571)270-7449. The examiner can normally be reached on Monday through Thursday 6:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Kim can be reached on (571)272-2293. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. I./
Examiner, Art Unit 2881

/ROBERT KIM/

Supervisory Patent Examiner, Art Unit 2881